UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/443,982	05/18/95	DIXIT V	20344210702O

18M2/0905

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EXAMINER	
ROMEO, D	
ART UNIT	**PAPER NUMBER**
1801	16

DATE MAILED: 09/05/97

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

☆U.S.GOVERNMENT PRINTING OFFICE 1995-319-826

Office Action Summary	Application No. 08/443,982	Applicant(s) Dixit et al.
	Examiner David Romeo 8/25/97 David Romeo	Group Art Unit 1801

☒ Responsive to communication(s) filed on *Jan 28, 1997*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-36* is/are pending in the application.

Of the above, claim(s) *7-20, 22, and 25-28* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-6, 21, 23, 24, and 29-36* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *15*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Formal Matters

1. The amendment filed 21 January 1997 (Paper No. 14) has been entered in full.

2. The previous Office action should have indicated that the preliminary amendment filed 18 September 1995 (Paper No. 5) had been entered instead of indicating that the amendments filed 22 February 1996 had been entered.

3. The drawings are considered to be informal because they fail to comply with 37 CFR 1.84(a)(1) which requires black and white drawings using India ink or its equivalent.

Photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) or (b)(1) is granted permitting their use as formal drawings. In the event applicant wishes to use the drawings currently on file as formal drawings, a petition must be filed for acceptance of the photographs or color drawings as formal drawings. Any such petition must be accompanied by the appropriate fee as set forth in 37 CFR 1.17(h), three sets of drawings or photographs, as appropriate, and, if filed under the provisions of 37 CFR 1.84(a)(2), an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

The file of this patent contains at least one drawing executed in color. Copies of this patent with color drawing(s) will be provided by the Patent and Trademark Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

4. The disclosure is objected to because of the following informalities: on page 6, line 12, "induces" is misspelled.

Appropriate correction is required.

5. Claim 23 is objected to because it depends from non-elected base claim 20. Appropriate correction is required.

6. The objection to the specification because the Brief Description of the Drawings failed to recite the appropriate sequence identifiers is withdrawn. Applicants' amendment has overcome this objection.

7. The objection to the specification because of failure to comply with the requirements of 37 CFR 1.821 through 1.825 is withdrawn. Applicants amendment has overcome this objection.

Election/Restriction

8. Applicant's election with traverse of Group I with traverse in Paper No. 14 is acknowledged. The traversal is on the ground(s) that it would not impart an undue search burden to examine Groups I, IV, V and IX together because all of the inventions of these Groups involve a search of the art for FADD proteins and a search for these proteins would reveal inhibitory agents, methods of synthesis, and methods of screening. Applicants arguments are persuasive with respect to the rejoining of Groups I, V, and IX. Claims 1-6, 21, 23, 24 and 29 to 36 will be examined on the merits. However, with respect to the rejoining of Group IV, claims 17 and 18, applicants arguments are not found persuasive because the claimed agent is independent and distinct both structurally and functionally from the specifically disclosed FADD protein, there is no requirement that it directly inhibit the binding of FADD to Fas, and there is no requirement that the claimed agent even be protein.

The requirement is still deemed proper and is therefore made FINAL.

Response to Arguments

9. The rejection of claim 1 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter, is withdrawn. Applicants' amendment to the claim has overcome this rejection.

10. The rejection of claims 1-6, 21, 23 and 24 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for FADD proteins identified by SEQ ID NO:2, does not reasonably provide enablement for a FADD protein, is maintained. The rejection of record is applied to claims 29 and 30 and to newly added claims 31 to 36. Applicant argues the specification defines FADD proteins in both structural and functional terms on page 13, lines 22 to 25. However, the only limitations recited in the cited definition is that FADD is a protein and that it modulates cellular function associated with Fas receptor pathway. Applicants also cite page 14, line 29 to page 15, line 7 as providing a structural definition of a FADD protein. However, the cited pages of the specification merely recite that a FADD protein can be a purified protein containing 208 amino acids and having a particular molecular weight as characterized by SDS-PAGE. The recited definition does not disclose with any degree of particularity what else a FADD protein "can" be. The other limitations implied by "can" are not disclosed. The claims encompass any structure that achieves the stated functional activity. It is not clear that the disclosure of a single species of FADD protein (SEQ ID NO:2) would enable the skilled artisan to make other structurally different proteins that have the same biological activity, or that structurally similar proteins would possess the desired biological activity, and the specification has not taught how to use a non-functional FADD protein. Because the specification has not enabled the full scope of the claimed FADD protein, it has also not enabled fragments of FADD, as recited in claims 3 to 5, 32 and 35, a process for chemically synthesizing a FADD protein or polypeptide,

as recited in claims 21 and 36, or a method for screening using FADD, as recited in claims 29 and 30.

11. The rejection of claims 3 to 5 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for AU1-N-FADD and FADDmt, does not reasonably provide enablement for fragments of FADD, is maintained. The rejection of record is applied to newly added claims 32 and 35. The claims are drawn to polypeptide fragments of FADD or to polypeptide fragments of FADD consisting of at least either the C-terminal or N-terminal portions of FADD. Applicants argue that on page 15, line 7 to page 16, line 16, the specification teaches how several different fragments of FADD can be used. Applicant argues on page 16, line 28 through page 17, line 29, the specification describes how FADD fragments can be made. Applicants argue the specification on page 50, lines 9-14 and on page 53, lines 1 to 18 the specification demonstrates how to make N- and C-terminal FADD fragments and how they function. However, because the claimed FADD encompasses any protein structure, as discussed *supra,* there are no structural limitation to the claimed fragments. Other than the full length FADD (SEQ ID NO:2) there are no working examples of a fragment of FADD that binds the cytoplasmic domain of a Fas receptor. For the skilled artisan to make a fragment of a protein of undefined amino acid composition and length that binds Fas would require excessive and undue experimentation. The specification discloses a fragment, N-FADD, and a single amino acid substitution mutant, FADDmt, which induce apoptosis but do not bind Fas (page 55, lines 17-23).

Thus, not all fragments of FADD (SEQ ID NO:2) bind Fas and fragments of SEQ ID NO:2 which induce apoptosis do not necessarily bind Fas. The specification has not disclosed the essential features of the FADD (SEQ ID NO:2) that confer binding to Fas or confer binding to Fas and induce apoptosis, which would enable the skilled artisan to construct fragments consisting of at least a portion of SEQ ID NO:2 that have the desired activity.

12. The rejection of claim 24 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn. Applicants' amendment has overcome this rejection.

13. Upon further consideration, the rejection of claims 1 to 6 and 20 under 35 U.S.C. 103(a) as being unpatentable over Itoh et al. al. (T) in view of Maekawa et al. al. (U), and further in view of Morrison et al. al. (V), is withdrawn.

Claim Rejections - 35 USC § 112

14. Claims 29 and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of screening for an agent that modulates the binding of FADD of SEQ ID NO:2 to the intracellular domain of the Fas receptor, does not reasonably provide enablement for a method of screening for an agent useful to modulate cellular function regulated by the Fas receptor pathway. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claimed method is drawn to a method of screening for an agent that modulates the cellular function regulated by the Fas receptor pathway. However, the method steps merely recite steps for determining the ability of an agent to inhibit the binding of FADD to Fas. There is no indication that an agent that inhibits said binding would be useful to modulate cellular function regulated by the Fas receptor. Further, the final step of the claimed method merely recites analyzing the results and does not achieve the purpose of the claim preamble. The specification has not enabled the skilled artisan to practice the claimed method without undue experimentation.

15. Claims 21, 23 and 31 to 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21 and 23 are indefinite because it is not clear if the "the protein or polypeptide" is the FADD protein or polypeptide recited in the preamble or some other protein or polypeptide. It is suggested that the phrase "said FADD protein or polypeptide" be used instead.

The phrase "non-naturally occurring" renders claims 31 to 36 indefinite because the claims include proteins not actually disclosed (those encompassed by "non-naturally occurring"), thereby rendering the scope of the claim unascertainable. Further, the claims do not provide a standard by which it could be determined whether a protein is naturally or non-naturally occurring.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claims 1 to 5 and 31 to 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Itoh (T, cited in previous Office action).

Claims are drawn to an isolated FADD protein characterized by having the ability to bind the cytoplasmic region of Fas receptor. There are no structural limitations to the claimed protein. Itoh et al. al. describe an isolated human Fas antigen (Figure 3, panel (b)) and a polypeptide fragment of the Fas antigen ((Figure 3, panel (c)), wherein the polypeptide fragment consists of at least the C-terminal portion of the protein (Figure 2, F58), and wherein the polypeptide consist of at least the N-terminal protein of the protein, (Figure 2, F58 and FD5) and characterized by the ability to induce apoptosis (page 10935, Figure 4, and column 1, second sentence). It is known in the art that the cytoplasmic domains of the Fas receptor self-associate and trigger apoptosis. Thus, the Fas receptor has the ability to bind the cytoplasmic regions of the Fas receptor and induce apoptosis, and the Fas receptor disclosed by Itoh et al. al. meets all the structural and functional limitations of the claimed FADD protein. Although the Fas receptor disclosed by Itoh et al. al. and the claimed FADD protein are different in name, the specification specifically intends

the term "FADD protein" to encompass analogs of FADD (Specification, page 14, lines 15-18). The Fas protein disclosed by Itoh et al. al. is such an analog.

18. Claims 6, 23, 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Itoh et al. al. (U1). The claims are drawn to a FADD protein or polypeptide, which has been recombinantly produced and isolated from a host cell. The specification defines a FADD protein or polypeptide as having the ability to modulate cellular function associated with Fas receptor pathway (page 13, lines 22-25). Itoh et al. al. disclose a Fas receptor which has been recombinantly produced and isolated from a host cell (Figure 3, page 236). The Fas receptor is protein or polypeptide that meets all the structural and functional limitations of FADD, as discussed *supra*. Although the Fas receptor and the claimed FADD protein are different in name, the specification specifically intends the term "FADD protein" to encompass analogs of FADD (Specification, page 14, lines 15-18). The Fas protein is such an analog. Although claims 23 and 24 are drawn to a product produced by a process, product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. The determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. Claims 21 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Itoh et al. al. (U1) in view of Berg et al. al. (A). The claims are drawn to a method of chemically synthesizing a FADD protein or polypeptide. Itoh et al. al. provide the amino acid sequence of the Fas receptor (page 235, Figure 2). The Fas receptor is protein or polypeptide that meets the structural and functional definition of a FADD protein or polypeptide, as discussed *supra*. Although the Fas receptor and the claimed FADD protein are different in name, the specification specifically intends the term "FADD protein" to encompass analogs of FADD (Specification, page 14, lines 15-18). The Fas protein is such an analog. Itoh et al. al. al. do not disclose a process for chemically synthesizing said Fas receptor.

Berg et al. al. al. disclose a method for the solid phase chemical synthesis of proteins in high yield and purity (column 15, line 50 to column 23, line 32). Berg et al. al. do not teach the chemical synthesis of a Fas protein.

It would have been obvious to one of ordinary skill in the art to chemically synthesize a Fas protein or polypeptide, as taught by Itoh et al. al., using the technique taught by Berg et al.

al., with a reasonable expectation of success. One of ordinary skill in the art would be motivated to chemically synthesize a Fas protein or polypeptide in order to produce a pure form of the protein or polypeptide with a minimum of purification steps.

The invention is *prima facie* obvious over the prior art.

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Conclusion

21. No claims are allowed.

22. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Boldin et al. al. (V1) disclose that the intracellular domain of the Fas receptor self-associates and triggers apoptosis (page 391, column 1).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David S. Romeo whose telephone number is (703) 305-4050. The examiner can normally be reached on Monday through Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephen Walsh, can be reached on (703) 308-2957.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to **[stephen.walsh@uspto.gov]**.

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

ELIZABETH C. KEMMERER
PATENT EXAMINER

David S. Romeo *DSR*
August 25, 1997